



LUITPOLD

April 3, 2006

Division of Dockets Management  
(HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, Room 1061  
Rockville, Maryland 20852

Re: CITIZEN PETITION – Generic Equivalents and Pharmaceutical  
Alternatives of Iron Sucrose Injection, USP  
Docket 2005P-0095

Dear Sir/Madam:

Reference is made to our Citizen Petition, Docket 2005P-0095/CP1, filed on March 4, 2005. Reference is also made to its FDA acknowledgement letter, dated March 7, 2005; our correspondence, dated March 23, 2005; and the Agency's interim response, dated August 31, 2005.

Luitpold Pharmaceuticals, Inc. respectively submits the enclosed addendum as further support of this petition requesting the Food and Drug Administration withhold approval of any Abbreviated New Drug Application or any 505(b) (2) application for any generic version or other pharmaceutical alternative of VENOFER® (iron sucrose injection, USP) unless and until any such applicant satisfies all of the conditions set forth in this Petition.

This addendum provides analytical comparison of four generic iron sucrose injections to VENOFER®. The testing was performed by Laboratorium für Arzneimittelprüfung und Zulassungsberatung (LAZ), a GLP/GMP contract testing laboratory located in Tuebingen, Germany. Attachment 1 provides a complete copy of their report.

The generic iron sucrose products tested were Feriv®, marketed in Spain by G.E.S. GENERICOS ESPAÑOLES, Hematin®, marketed in Latin America by Laboratorios Chalver, Fe-Back®, marketed in Taiwan by N.K. (Nang Kuang), and Fe-Lib®, marketed in Taiwan by AIPN (Advanced International Pharmaceutical Nanotech Inc.). A copy of Feriv®'s carton labeling and accompanying translation

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is provided in Attachment 2 and a copy of Hematin®'s carton labeling and accompanying translation is provided in Attachment 3.

Though these drug products are not purported to be related to any specific submission, this data is being provided to aid the Agency in its review of any pending or future ANDA and/or 505(b) (2) submissions for any generic version or other pharmaceutical alternative of VENOFER® (iron sucrose injection, USP).

This analysis was sponsored by our API manufacturer of VENOFER®, Vifor (International) Inc. The test methods and parameters were as per iron sucrose injection's USP monograph requirements for pH, alkalinity, turbidity, molecular weight determination, limit of iron (II) and redox potential [Polarography <801>].

In addition, VENOFER®'s *in vitro* release test for trivalent iron was performed and is reported by LAZ as "kinetics of degradation ( $T_{75}$ )."  
This test method was developed in fulfillment of our NDA Phase IV commitment. This test method and examples are disclosed in US patent number 6,911,342; *Helenek, et al.*  
"Bioequivalence test for iron-containing formulations."

In regard to the aforementioned tests, LAZ found the batches of the copy products Feriv®, Hematin®, Fe-Back®, and Fe-Lib®, failed to comply with the USP monograph for Iron Sucrose Injection or with the registered specification of Venofer®. Moreover, significant differences in the robustness and the redox potential of the iron sucrose complex between Venofer® and these copy products were detected. The recorded differences of some physicochemical characteristics clearly indicate a different API manufacturing process and different compositions and structures of Feriv®, Hematin®, Fe-Back®, and Fe-Lib® in comparison to Venofer® as outlined in the enclosed report of LAZ (Attachment 1).

Though Feriv®, Hematin®, Fe-Back®, and Fe-Lib® are not marketed in the United States; these products are considered generic equivalents to VENOFER® in Spain, Latin America and Taiwan, respectively. The data in this addendum is provided to illustrate to the Agency VENOFER®'s USP specifications collectively define both the API and the finished product, specifically its composition, particle size, turbidity point and reduction potentials.

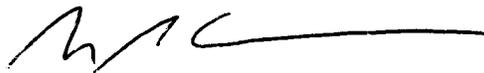
Clearly Feriv®, Hematin®, Fe-Back®, and Fe-Lib® are not generic equivalents to VENOFER® as defined in Section 505(j)(2)(A)(i)(I) of the Act. Therefore, the Agency should establish guidelines for approval of parenteral iron colloidal suspensions referencing VENOFER® as the RLD and other parenteral iron colloidal suspensions, such as FERLECIT®, prior to approving any generic or 505(b) (2) application for any such product. Such guidelines should include, at a minimum, requirements for:

- (1) Demonstrating the identity of the manufacturing process of the API and the finished product to those of the RLD and its API;
- (2) The submission of validated methods and data demonstrating complete pharmaceutical equivalence, including identity of the colloidal structure and stability of the complex thereof;
- (3) A requirement for generic applicants to conduct bioequivalence studies and for 505(b) (2) applicants to submit complete preclinical and clinical data for each proposed indication;
- (4) A requirement for generic and 505(b)(2) applicants to develop and submit an *in vitro* release test for demonstration of batch to batch bioequivalence; and
- (5) A requirement for 505(b)(2) applicants to conduct safety studies in at least 1,000 patients and for their labeling to bear a bolded and/or boxed warning appropriate to the amount and type of information about the product.

Until the Agency establishes such guidelines for parenteral iron colloidal suspensions, it should not approve any generic or pharmaceutical alternative of such product.

Sincerely,

Luitpold Pharmaceuticals, Inc.



Richard P. Lawrence  
Director, Research and Development